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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/895,975 | 06/29/2001 | Mark R. Schmitt | AM100341 | 9267 |

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| EXAMINER | |
|---|---|
| TRUONG, TAMTHOM NGO | |
| **ART UNIT** | **PAPER NUMBER** |
| 1624 | |

DATE MAILED: 12/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/895,975 | SCHMITT ET AL. | |
| | Examiner | Art Unit | |
| | Tamthorn N. Truong | 1624 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *28 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2-4,6-8,10-12,14-20,22,67,74-77,79-81,83-85,87-93 and 95-97* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4,6-8,10-12,14-20,22,67,74-77,79-81,83-85,87-93 and 95-97* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's amendment of 09-28-04 has been fully considered. The amended claims have overcome the previous rejection of 112/2nd paragraph by inserting substituents following the phrase "*optionally substituted*", and by deleting the phrase "*and associated diseases*". The cancellation of claim 70 has also overcome the previous ODP rejection. However, in reviewing the evidence provided in the specification, the following "Scope of Enablement" is necessary.

Claims 1, 5, 9, 13, 21, 23-66, 68-73, 78, 82, 86, and 94 have been cancelled.

Claims 2-4, 6-8, 10-12, 14-20, 22, 67, 74-77, 79-81, 83-85, 87-93, and 95-97 are pending.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**Scope of Enablement:** Claims 2-4, 6-8, 10-12, 14-20, 22, 67, 74-77, 79-81, 83-85, 87-93, and 95-97 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of lung cancer, gliobastoma, melanoma, and colon cancer, does not reasonably provide enablement for the treatment of other types of cancer, or the treatment of cancerous cells that express multiple drug resistance (MDR). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

**The breadth of the claims:**

**a.** Claims 2 recites: "A method of treating or inhibiting the growth of cancerous tumor cells…", which covers broadly the treatment of all types of cancers. Claims 3, 4, 6-8, 10-12, 14-20, 22 are dependent on claim 2, but they recite subgenera or species of formula (I).

**b.** Claim 67 recites specific cancerous tumor cells such as: breast, colon, lung, prostate, melanoma, epidermal, leukemia, kidney, bladder, mouth, larynx, esophagus, stomach, ovary, pancreas, liver, skin, and brain. Such a list covers more cancers and tumors than the guidance provided in the specification.

**c.** Claim 75 recites: "A method for the treatment or prevention of cancerous tumor cells that express multiple drug resistance (MDR)...", which covers cancers that are resistant to an unknown number and types of drugs.

**d.** Claims 74, 76, 77, 79-81, 83-85, 87-93, and 95-97 are dependent on claim 75.

**e.** All these claims are drawn to a broad scope of treatment using a large number of compounds represented by formula (I).

**The amount of direction or guidance presented:** The specification provides bioassays on human leukemia cells, Hela cells, Non-small lung carcinoma cells, glioblastoma cells, melanoma cells, and colon carcinoma cells. In said bioassays, only a handful of compounds are tested for apoptosis (from an increase of G2/M phase), tubulin polymerization, and their effect on the mitotic spindle microtubules. However, the effect on such a limited number of cell types cannot be extrapolated to other cancerous cells such as those of liver, kidney, pancreas, prostate, bladder, mouth, larynx, esophagus, stomach, ovary, breast, etc. Those cancerous cells do not have the same manifestation as the ones tested, and may even be related to hormones. Therefore, merely showing the general effect of apoptosis, tubulin polymerization, and mitotic spindle microtulules does not sufficiently guide the skilled clinician to treat cancers that are beyond those tested cancerous cell lines.

The specification does not provide any evidence for the treatment of cancerous cells that resist multiple drugs. Thus, there is no enablement for the treatment recited in claim 75.

**The state of the prior art:** Currently, many chemo agents can treat certain types of solid tumors, or cancers such as: non-small lung carcinoma, colon cancer, melanoma, breast and

prostate cancers if they are detected early. For cancers such as: liver, kidney, stomach, pancreas, brain, which tend to metastasize quickly, and are more difficult to treat.

**The relative skill of those in the art:** Those skilled in the art usually have advance training of either an MD or a Ph. D degree. However, even with such advance training, the skilled clinician would have to carry out a pharmacokinetic profile for each of the claimed compounds as well as establishing a therapeutic index, and $LD_{50}$ for each of them. In addition, more cell lines would need to be tested. Such a task requires more than routine experimentation.

**The predictability or unpredictability of the art** and **The quantity of experimentation necessary**: The pharmaceutical art in general is very unpredictable, especially the treatment of cancers. The *in-vitro* effect does not always warrant the same *in-vivo* effect. Also, for a large group of compounds such as the instant formula (I), a handful of compounds having activity does not guarantee the same activity for other compounds of the same genus.

Therefore, with the limited guidance provided and the large genus claimed herein, undue experimentation is inevitable for the skilled clinician to practice the invention beyond the treatment of a few cancers supported by the specification.

***Reference on PTO-892***

The references cited on PTO-892 shows state of the art. The analogous compounds mostly have fungicidal activity, cardiovascular activity, and neurological activity.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (10:00-6:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

***Tamthom N. Truong***
***Examiner***
***Art Unit 1624***

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12-07-04